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Barium Bioavailability as the Chloride, Sulfate, or Carbonate Salt in the Rat

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16. ABSTRACT

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BARIUM BIOAVAILABILITY AS THE CHLORIDE, SULFATE, OR CARBONATE SALT IN THE RAT

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ABSTRACT

This study was conducted to determine how the bioavailability of a low concentration of barium (Ba) in drinking water is affected by the anion. Male Sprague Dawley rats weighing 250-300 grams were maintained on a diet of less than 1 mg Ba/kg of food for at least 1 month prior to experimentation. Rats were given 10.0 mg ^{131}Ba/liter as sulfate (SO_4), chloride (Cl), or carbonate (CO_3) at pH 7.0. Animals were sacrificed at 2, 5, 10, 20, 30, 60, and 120 minutes and 24 hours after intubation. When ^{131}Ba was administered, as Cl, ^{131}Ba in blood rose linearly for 10 minutes and then less rapidly until the highest number of counts was measured at 60 minutes. At 24 hours ^{131}Ba was still at 90% of peak levels. Five tissues were tested 24 hours after dosing for ^{131}Ba. In decreasing order of ^{131}Ba concentration they were heart, eye, skeletal muscle, kidney, and liver. ^{131}Ba in the heart reached 8x that observed in blood 24 hours after dosing. In the eye, ^{131}Ba increased linearly for 1 hour. Isotope concentrations in the eye eventually reached 2.5x that observed in blood. When ^{131}Ba was administered as SO_4 or CO_3, ^{131}Ba in blood was respectively 85% or 45% of levels, of ^{131}Ba from $^{131}BaCl_2$. Initial uptake of ^{131}Ba and deposition in the eye were not different when administered as Cl or SO_4.

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INTRODUCTION

In certain ground water aquifers, barium (Ba) concentrations exceed 20 mg/l.[1] It is not clear whether ground water Ba exists as ionized Ba ($BaCl_2$) or as a suspension ($BaCO_3$ or $BaSO_4$). It probably is a complex mixture of anion species.

To determine the bioavailability of Ba from such sources ^{131}Ba was used in order to establish the possibility of a health risk due to chronic exposure. Three salt forms found in ground water were used to compare relative rates of gastrointestinal absorption. ^{131}Ba was measured in blood to help determine the relative rates of absorption among Ba salts. ^{131}Ba measurements in the eye were conducted to indicate the realtive distribution rats. The eye was picked for sampling because is is easy to excise and is know to concentrate Ba.[2]

METHODS

Male Sprague Dawley rats of 250-300 g were maintained on a diet of less than 1 mg Ba/kg of food for at least 1 month prior to experimentation. Overnight (24 hours) fasted rats were given 10.0 mg ^{131}Ba liter as chloride (pH 7.0) by intubation (0.5 ml/100 g body weight). Fasted rats were sacrificed at 2, 15, 30, 60, 120, and 480 minutes after intubation. Blood was sampled by 200 ul capillary tube and eyes were placed in tared scintillation vials. Ad Lib fed rats received 10.0 mg ^{131}Ba as SO_4, Cl_2, or CO_3 at pH 7.0 by intubation (0.5 ml/100 g body weight). Fed rats were sacrificed at 2, 5, 10, 20, 30, 60, 120 minutes and 24 hours.

Blood and eyes were sampled as described above. Fed rats which received $^{131}BaCl_2$ for 24 hours were dissected; whole heart, one lobe of the liver, both kidneys, and the rostral thigh muscle were excised and placed in tared scintillation vials. All samples were counted in a Packard auto-gamma scintillation spectrometer (model CP 15-3). All counts were adjusted for decay.

^{131}Ba was purchased as ^{131}BaO. $^{131}BaCl$ was prepared by dissolving 1.25 mg ^{131}BaO with 1 ml 6 N HCl and diluted to 10 ml. This solution was neutralized to pH 7.0 with NaOH and diluted to 10 mg ^{131}Ba/liter final concentration with distilled water. $^{131}BaSO_4$ was prepared by solubilization 1.25 mg ^{131}BaO with 1 ml concentrated H_2SO_4 and then diluted with distilled water and neutralized with NaOH. Dilution to 10 mg ^{131}Ba/l resulted in the appearance of a fine white precipitate. Therefore, dosing solutions were shaken immediately before each dosing. $^{131}BaCO_3$ was prepared by solubilizing 1.0 mg ^{131}BaO with 1 ml 6 N HCl. The sample was diluted to 9 ml with distilled H_2O and further diluted to 90 ml with 1 M Na_2CO_3. The sample was neutralized with concentrated HCl and taken to final volume (100 ml) with distilled water.

RESULTS

Fasted rats which received $^{131}BaCl_2$ by intubation demonstrated the highest blood ^{131}Ba level 15 minutes after dosing (Figure 1). This was the highest ^{131}Ba concentration measured at any time in any dosing group. Blood ^{131}Ba levels declined to about 50% of this high level after 4 hours.

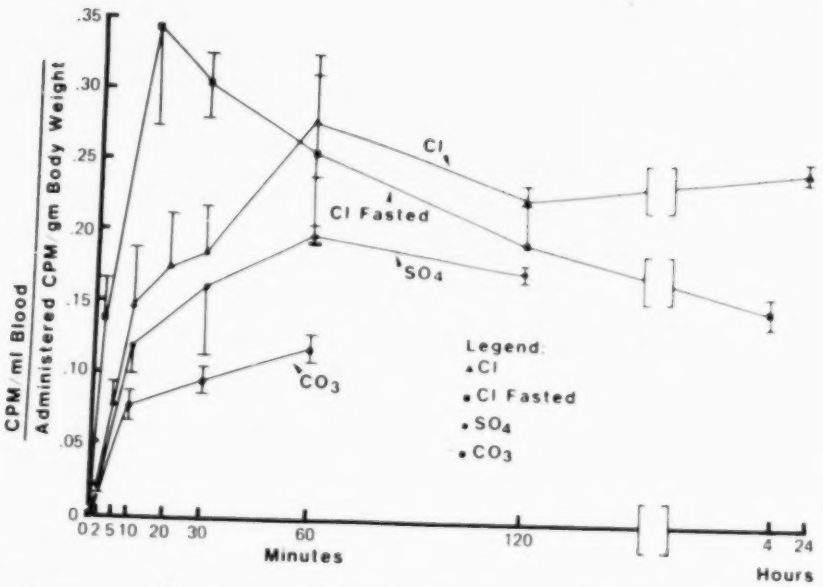

Figure 1. ^{131}Ba concentrations in blood at various time intervals after intubation with ^{131}Ba. Fasted rats were dosed 24 hours after food was withdrawn. All animals were dosed by intubation at the rate of 5 ml/kg of a solution containing 10 mg ^{131}Ba/liter as barium chloride (Cl), sulfate (SO_4), or carbonate (CO_3). At the specified time interval animals were sacrificed and blood was sampled using a 200 ul capillary tube. Each point represents the average of 6 rats. The standard error of the mean (SEM) is represented by cross bars.

Fed rats receiving $^{131}BaCl_2$ demonstrated their highest blood ^{131}Ba concentrations at 60 minutes after dosing. ^{131}Ba accumulation curves similar are in shape in fed rats receiving ^{131}Ba as either Cl, SO_4, or CO_3. However, animals receiving $^{131}BaSO_4$ demonstrated 80 to 90% of the blood ^{131}Ba levels of animals receiving $^{131}BaCl_2$ for similar time periods. $^{131}BaCO_3$ dosed animals only accumulated 40-50% the blood ^{131}Ba levels of $^{131}BaCl_2$ dosed animals.

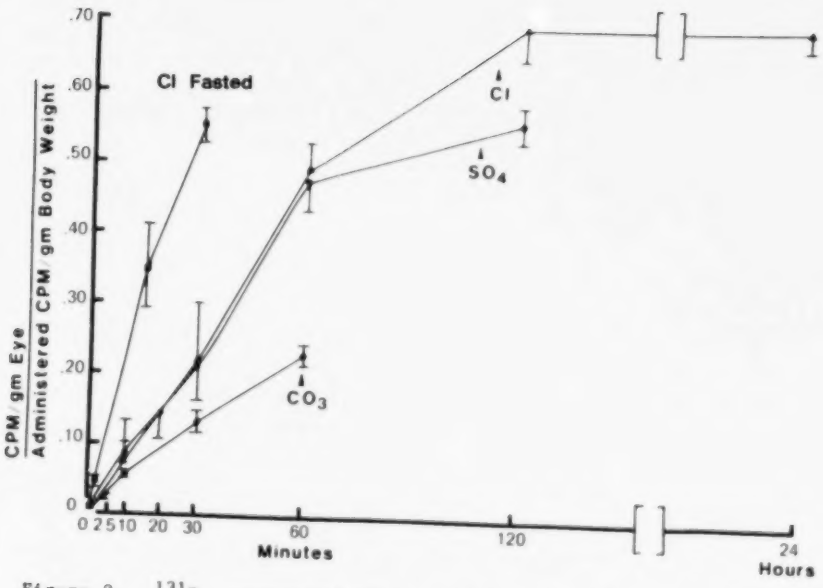

Figure 2. ^{131}Ba concentrations in eye at various time intervals after intubation. Fasted rats were dosed 24 hours after food was withdrawn. All animals were dosed by intubation at the rate of 5 mg/kg of a solution containing 10 mg ^{131}Ba/liter of barium chloride (Cl), sulfate (SO_4), or carbonate (CO_3). At the specified time interval animals were sacrificed and eyes were excised for ^{131}Ba counting. Each point repesents the average of 6 rats. The standard error of the mean (SEM) is represented by the cross bars.

This highest rate of ^{131}Ba accumulation in eyes was recorded in fasted rats receiving $^{131}BaCl_2$. This ^{131}Ba level increased linearly over 30 minutes (Figure 2).

In fed rats, ^{131}Ba levels in eye rose linearly for the first hour. Concentrations were nearly identical in rats dosed with $^{131}BaCl_2$ and $^{131}BaSO_4$. Rats receiving $^{131}BaCO_3$ accumulated ^{131}Ba in the eye at about 50% of the rate of $^{131}BaCl_2$ and $^{131}BaSO_4$ for the first hour. During the second hour, rats receiving $^{131}BaCl_2$

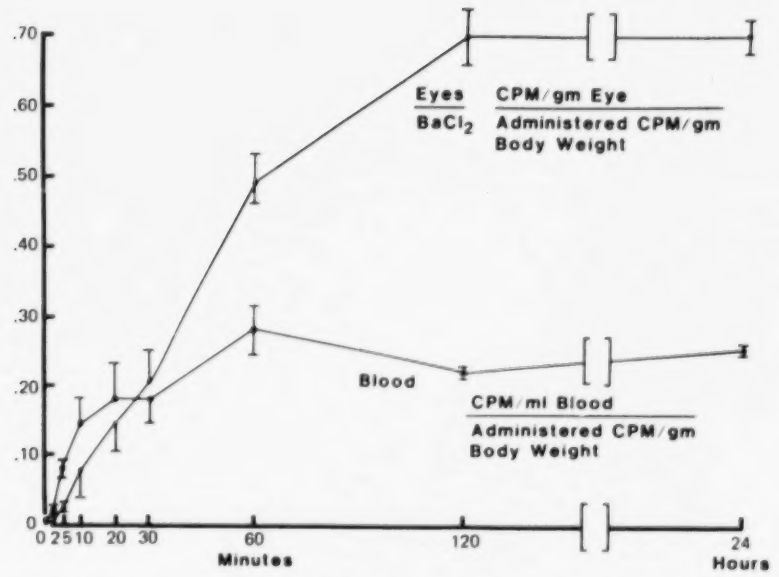

Figure 3. A comparison of ^{131}Ba concentations in eye and blood at various time intervals after intubation. Animals were dosed by intubation at the rate of 5 mg/kg of distilled water solution containing 10 mg ^{131}Ba as $BaCl_2$. At the specified time intervals blood was sampled and eyes excised for counting purposes. Each point represents the average of 6 rats. The standard error of the mean (SEM) is represented by the cross bars.

continued to increase ^{131}Ba concentrations in eye, but the ^{131}Ba levels did not increase after 2 hours for dosing (Figure 2).

Figure 3 illustrates the relationship between of ^{131}Ba levels in blood and eye when animals are intubated with $^{131}BaCl_2$. ^{131}Ba concentrations in eye were below the concentrations in blood until 30 minutes after dosing. At 1 hour they were nearly twice blood levels (Figure 3). ^{131}Ba concentration in blood plateaued after 1 hour and in eyes after 2 hours. ^{131}Ba blood and eye concentrations remained constant for 24 hours after dosing. Plateau ^{131}Ba

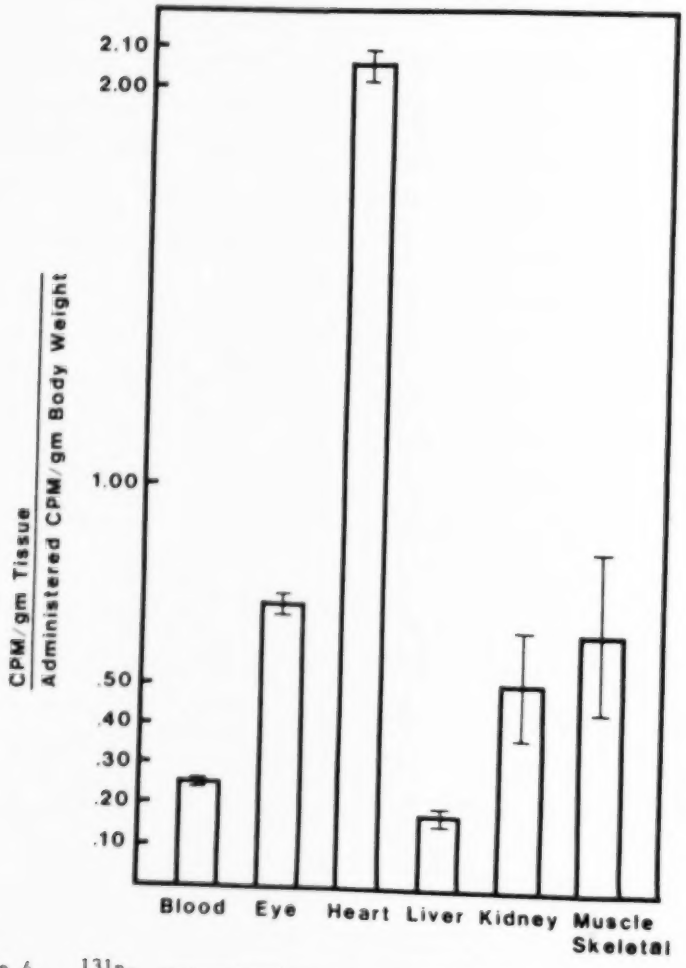

Figure 4. ^{131}Ba concentrations in 6 tissues 24 hours after intubation. All animals were sacrificed 24 hours after dosing with 5 ml/kg of 10 mg ^{131}Ba/liter as $BaCl_2$. Tissues were excised and counted in tared scintillation vials. Each bar represents the average of 6 animals and the standard error of the mean is represented by the cross bar.

levels in eye were equivalent to nearly 3-fold blood ^{131}Ba concentration.

Tissue concentration of ^{131}Ba in $^{131}BaCl_2$ dosed fed rats were highest in cardiac muscle. They were 3 times higher than the next highest tissue (eye) (Figure 4). Eye, skeletal muscle, and kidney were nearly equivalent in ^{131}Ba concentration. Of the 5 tissues tested, only liver demonstrated lower ^{131}Ba concentrations than blood (70% of blood concentration).

DISCUSSION

Oral doses of $BaSO_4$ are used clinicaly as a radiopaque aid to x-ray diagnosis. When $BaSO_4$ is administered in large doses, very small fractions are absorbed. When $BaCl_2$ is administered in large oral doses, it is readily absorbed and causes a digitalis-like toxicity.[3]

Although large doses of $BaSO_4$ are poorly absorbed, acid in the stomach could easily solubilize small quantities of $BaSO_4$ in gastrointestional track. The degree to which a small finely divided precipitate of Ba, such as $BaSO_4$ or $BaCO_3$, is absorbed is more relevant to chronic toxicity of Ba as it is encountered in drinking water.

When ^{131}Ba is administered to rats in concentrations of 10 mg/liter at the dose rate of 5 ml/kilogram of body weight, $^{131}BaSO_4$ and $^{131}BaCl_2$ are absorbed by fed rats at nearly equivalent rates. $^{131}BaCO_3$ was administered in a vehicle containing 0.8 M $NaHCO_3$, pH 7.0, and was more poorly absorbed. This lower absorption rate may be due, at least in part, to the large buffering capacity of

0.8 M $NaHCO_3$. This may prevent hydrochloric acid mediated conversion to $BaCl_2$.

^{131}Ba was absorbed into eye in fed or fasted rats in a similar fashion (relative to blood barium concentrations) regardless of the anion species used in dosing. In all cases, relative ^{131}Ba concentrations were at least 2-fold higher in eye than in blood at the last time period measured. When ^{131}Ba was determined in 5 tissues 24 hours after dosing, 4 out of 5 tissues demonstrated 2-8x the ^{131}Ba concentration relative to that found in blood. This demonstrates that $^{131}BaCl_2$ is not only absorbed, but at least in some tissue compartments is concentrated over whole blood levels. Based upon the similar fashion in which ^{131}Ba administered as Cl, SO_4 or CO_3 is distributed in to eye one might assume that ^{131}Ba administered as $^{131}BaSO_4$ or $^{121}BaCO_3$ would distribute to heart, liver, kidney, and skeletal muscle as does ^{131}Ba from $^{131}BaCl_2$.

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